EXHIBIT A

Declaration of Prof. Gregory B. Dudley, Ph.D.

BACKGROUND

1. I am the Eberly Family Distinguished Professor and Department Chair of the C. Eugene Bennett Department of Chemistry at West Virginia University in Morgantown, WV. Prior to this appointment, I was a Professor and Associate Chair in the Department of Chemistry and Biochemistry at Florida State University (FSU) in Tallahassee, FL, and member of the Graduate Faculty in the College of Pharmacy and Pharmaceutical Science at Florida A&M University (FAMU) in Tallahassee, FL.

2. I graduated *magna cum laude* with a B.A. in Chemistry from FSU in 1995, and I earned a Ph.D. in Organic Chemistry from the Massachusetts Institute of Technology (MIT) in 2000. I then received a National Institutes of Health (NIH) Fellowship to conduct postdoctoral research in Molecular Pharmacology and Chemistry at the Sloan–Kettering Institute for Cancer Research, the research wing of the Memorial Sloan–Kettering Cancer Hospital in New York, NY. I worked in this capacity from 2000–2002, at which point I accepted an Assistant Professor position at FSU. I was promoted to Associate Professor with tenure in 2008 and Professor in 2015.

3. My research efforts have produced over 70 peer-reviewed publications, 7 invited contributions to leading reference works in organic chemistry, and multiple patents for innovations leading to two commercial products.

4. I have been called upon frequently to provide expert peer-review services for leading journals in chemistry (e.g., *Journal of the American Chemical Society*), organic chemistry (e.g., *The Journal of Organic Chemistry*), and medicinal chemistry (e.g., *ACS Medicinal Chemistry*) and major research funding agencies (e.g., National Institutes of Health, National Science Foundation, American Chemical Society). I have delivered well over 100 invited lectures at universities, scientific conferences, and pharmaceutical companies. I have received numerous awards and recognition related to research, teaching, and innovation in chemistry.

5. I am an independent consultant specializing in organic chemistry and related fields. I have provided expert opinion reports, analysis, and/or testimony on the scientific considerations relevant to Controlled Substance Analogue determinations and other similarity comparisons on multiple occasions.

6. I have consulted on dozens of cases related to designer drugs and the Analogue Enforcement Act, testified on numerous occasions in Federal and State courts, and given professional development seminars and panel presentations on molecular and pharmacological similarity comparisons to conventions of attorneys.

7. I have lectured on molecular similarity comparisons at regional and national meetings of the American Chemical Society.

8. I contributed to an *Amicus Brief* submitted to the Supreme Court of the United States in the case of *McFadden v. United States of America*.

9. I have provided written and oral testimony by invitation on two occasions to the United States Sentencing Commission on the topic of emerging designer drugs.

10. My credentials and experience are outlined in my CV.

SUMMARY OPINION

11. U-47,700 is not substantially similar in chemical structure to AH-7921.

    a. U-47,700 has a ***different core structure*** and ***different chemical functionality*** compared to the controlled substance, with atomic connectivity changing in such manner that functionality existing in AH-7921 is eliminated in U-47,700.

12. Furanyl fentanyl is not substantially similar in chemical structure to fentanyl.

    a. Furanyl fentanyl has a ***different core structure*** compared to the controlled substance.

13. Acryl fentanyl is not substantially similar in chemical structure to fentanyl.

    a. Acryl fentanyl has ***different chemical functionality*** (new functional group) compared to the controlled substance.

14. *Core structure* and *functional groups* are defining features of chemical structures and primary considerations of structure-based comparisons for regulatory controls.

BASIS AND RATIONALE[1]

15. I have reviewed published literature on similarity comparisons, including molecular similarity comparisons, and on the significance and impact of various changes in chemical structure.

16. Analogue determinations require subjective similarity comparisons of molecular substances, which are impossible to accomplish objectively and consistently: "*it cannot be said with certainty if two compounds are similar to each other.*"[2]

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1. *Technical note*: The molecular structures of substances discussed herein are graphically depicted using two-dimensional line drawing notation, in accord with standard practices in organic chemistry. The reference synthetic cannabinoid is illustrated in **red**, and the alleged chemical analog is illustrated in **black**.

2. Maggiora, Gerald M., Martin Vogt, Dagmar Stumpfe, and Jürgen Bajorath. "Molecular Similarity in Medicinal Chemistry." *Journal of medicinal chemistry* 57 (2014), 3186–3204.

17. There is no statutory definition of "substantially similar", nor is there any scientifically accepted standard, definition, or measure for determining the scope of analogue comparisons.[3]

18. Although there can be no objective measure of "substantially similar", in my opinion the following if/then statement can help define an appropriate scope of coverage and guide consistent determinations:
If substances that are "*substantially similar*" can be subjected to the same regulatory controls, then "*substantially similar*" means *similar enough to be subjected to the same regulatory controls*.

19. Changes to core framework features and/or chemical functional groups are generally regarded as significant in medicinal chemistry.

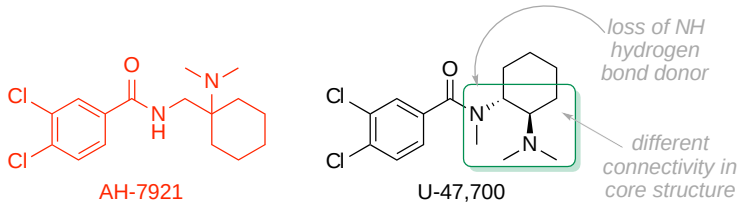
20. Changes to core framework features and/or chemical functional groups are also regarded as significant in the context of regulatory controls, as exemplified by the statutory definition of "positional isomer", in which any change of core structure or chemical functionality / functional groups is disqualifying (emphasis added):
"*the term "positional isomer" means any substance possessing the same molecular formula and core structure and having the same functional group(s) and/or substituent(s)* [attached] *in such manner that no new chemical functionalities are created and no existing chemical functionalities are destroyed…*"[4]

    a. As with the regulatory identification of controlled substance analogues, the regulatory identification of positional isomers requires subjective comparison of chemical structures.
    b. The regulatory guidance is to consider "*core structure*" and "*functional group(s)*" when making subjective positional isomer determinations, in addition to the objective consideration of the substances "*having the same molecular formula*".
    c. It is similarly appropriate to consider *core structure* and *functional group(s)* when making subjective Analogue determinations, because core structure and functional groups are the defining structural features that determine properties of a molecular substance.

21. Chemical structures having different core structures or different functional groups and/or chemical functionalities are not substantially similar, because they differ in significant ways.

3. Ralph Little and Shannon MacGillis, *Synthetic Drug Compounds — The Need for a Systematic Approach*. North Florida High Intensity Drug Trafficking Area position paper, November 17, 2014.
4. From: Definition of ''Positional Isomer'' as It Pertains to the Control of Schedule I Controlled Substances. 21 CFR Part 1300 [Docket No. DEA–260F] Federal Register / Vol. 72, No. 231 / Monday, December 3, 2007.

U-47,700



22. In my opinion, the substance U-47,700 should not be treated as Controlled Substance Analogue of AH-7921, because these two substances are not "substantially similar" in chemical structure.

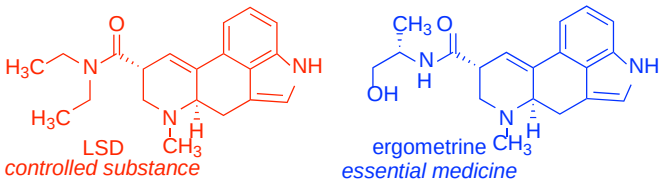
23. U-47,700 differs in chemical structure from AH-7921 by a change in the *core structure*.

    a. AH-7921 features a 1-aminomethylcyclohexylamine where U-47,700 has a *trans*-1,2-cyclohexanediamine.
    b. The differences in core structure mean that these two substances cannot achieve an appropriately similar shape to support similar molecular interactions, including with large biomolecules of relevance to understanding drugs of abuse.

24. U-47,700 differs in chemical structure from AH-7921 by a change in the *chemical functionality / functional group*.

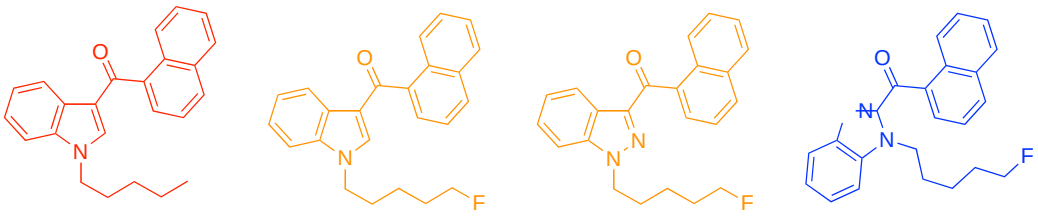
    a. AH-7921 is a secondary amide where U-47,700 is a tertiary amide.
    b. Therefore, AH-7921 is a hydrogen bond donor whereas U-47,700 is not.
    c. Hydrogen bonding is one of the fundamental mechanisms of molecular interactions, including with biomolecules of relevance to drugs of abuse.

25. These differences in chemical structure are significant; AH-7921 and U-47,700 are not substantially similar in chemical structure.



26. For context in Analogue determinations, consider that the *chemical functionality / functional group* difference in chemical structure between AH-7921 and U-47,700 is analogous to — but arguably greater than — the difference between LSD and ergometrine.

    a. LSD is a Schedule I controlled substance associated with hallucinations. Ergometrine is a World Health Organization-designated essential medicine for assisting with labor and delivery in pregnant mothers-to-be.
    b. Ergometrine is a secondary amide with an additional alcohol functional group, whereas LSD is a tertiary amide.



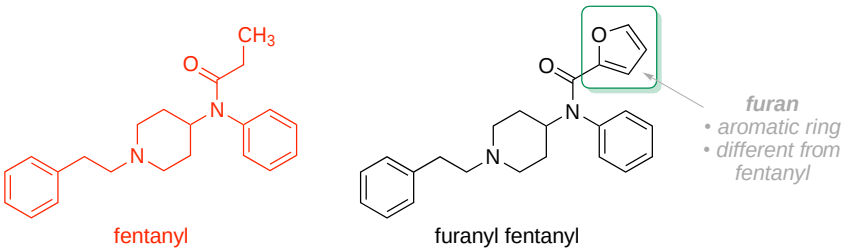
27. For context in Analogue determinations, consider that the *core structure* difference in chemical structure between AH-7921 and U-47,700 is analogous to — but arguably greater than — the difference between JWH-018 and FUBIMINA.

    a. According to DEA testimony,[5] the synthetic cannabinoid FUBIMINA does not meet their controlled substance analogue criteria because it is not "substantially similar" in chemical structure to a controlled substance (i.e., JWH-018).
    b. JWH-018 is a Schedule I controlled substance and one of the original synthetic cannabinoid ingredients in illicit synthetic marijuana products.
    c. AM-2201 and THJ-2201 are synthetic cannabinoids regarded by the DEA ODE as "substantially similar" in chemical structure to a controlled substance (i.e., JWH-018 and AM-2201, respectively).
    d. FUBIMINA differs from the others in core structure.

28. Considering that AH-7921 and U-47,700 are not substantially similar in chemical structure — they have different core structures and different chemical functionality — they should be regulated independently.

29. In my opinion, U-47,700 is not a controlled substance analogue of AH-7921 by virtue of Prong 1 considerations: they are not "substantially similar" in chemical structure.

Furanyl fentanyl

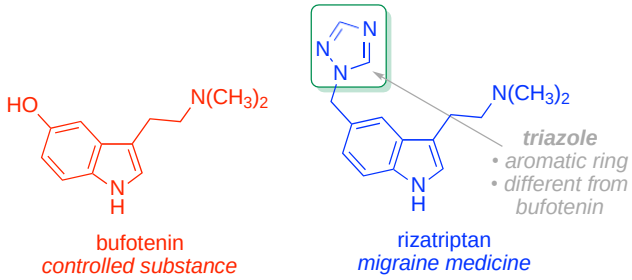


30. In my opinion, the substance furanyl fentanyl should not be treated as a Controlled Substance Analogue of fentanyl, because these two substances are not "substantially similar" in chemical structure.

31. Furanyl fentanyl differs in chemical structure from fentanyl by a change in the *core structure*.

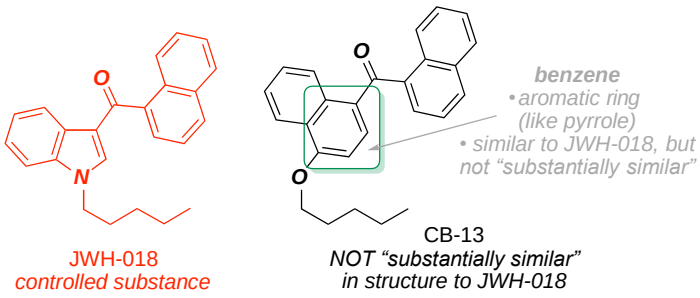
5. *US v. Broombaugh*, 5:14-cr-40005-DDC.

a. Differences in core structure are associated with different size, shape, and conformational dynamics of the molecules.
b. Furanyl fentanyl has an extra ring system as compared to fentanyl, and this ring system is *aromatic*.
c. Aromatic rings (e.g., furan) are associated with specific patterns of reactivity and binding interactions that are not available to alkyl (e.g. ethyl) groups.
d. Alkyl groups, particularly when attached to a carbonyl as is the ethyl group in fentanyl, are associated with specific patterns of reactivity and binding interactions that are not available to aromatic rings.



32. For context in Analogue determinations, consider that the *core structure* difference in chemical structure between fentanyl and furanyl fentanyl is analogous to (although arguably less than) the difference between bufotenin and rizatriptan (Maxalt).

a. Bufotenin is a Schedule I controlled substance associated with hallucinogenic toads and mushrooms. Rizatriptan (Maxalt) is an unscheduled prescription medicine prescribed for migraine headaches.
b. Rizatriptan (Maxalt) has an extra ring system as compared to bufotenine, and this ring system is *aromatic*.



33. For context in Analogue determinations, consider that the *core structure* difference in chemical structure between fentanyl and furanyl fentanyl is arguably greater than the difference between JWH-018 and CB-13.

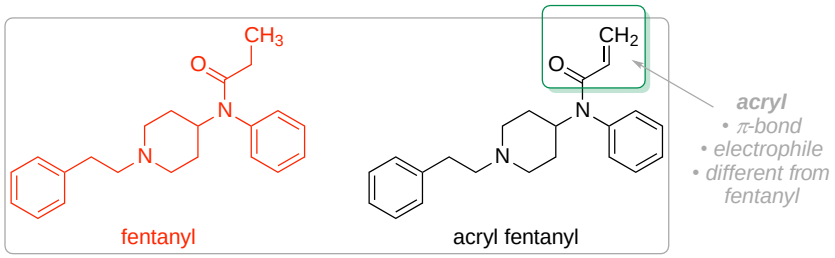
a. JWH-018 is a Schedule I synthetic cannabinoid controlled substance. CB-13 is also a synthetic cannabinoid.

b. According to DEA testimony,[6] CB-13 "didn't meet the definition of being substantially similar in chemical structure" to JWH-018.
c. CB-13 has a different aromatic ring as compared to JWH-018, with an oxygen atom to off-set the differences in shape and binding interactions between the two aromatic rings.[7]
d. The structure of CB-13 was designed to mimic JWH-018 in its size, shape, and binding interactions, but with the significant change of replacing one aromatic ring with another (i.e., similar but not "substantially similar").
    i. As noted by the designers of CB-13, the aromatic rings of JWH-018 and CB-13 are similar in size, shape, and binding interactions. In their words, "we replaced the indole ring system with a naphthalene one, as previous work… had demonstrated a bioisosteric equivalency between indole and naphthalene".[7]
    ii. If replacing one aromatic ring with another of similar size, shape, and binding interactions is significant, then so is replacing an alkyl group with an aromatic ring.

34. In summary, it is my opinion that furanyl fentanyl is not substantially similar in chemical structures to fentanyl.

    a. The core structures of these two substances differ in a significant way.
    b. The furanyl portion of furanyl fentanyl is significant.
    c. If there is a significant difference between two structures, then the structures are not "substantially similar".

Acryl fentanyl



35. In my opinion, the substance acryl fentanyl should not be treated as a Controlled Substance Analogue of fentanyl, because these two substances are not "substantially similar" in chemical structure.

36. Acryl fentanyl differs in chemical structure from fentanyl by a change in the *chemical functionality / functional group*.

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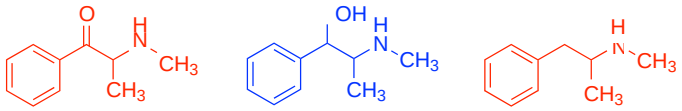
6. *US v. Fedida*, 6:12-cr-209-Orl-37DAB.

7. Dziadulewicz, Edward K., Stuart J. Bevan, Christopher T. Brain, Paul R. Coote, Andrew J. Culshaw, Andrew J. Davis, Lee J. Edwards et al. "Naphthalen-1-yl-(4-pentyloxynaphthalen-1-yl) methanone: a potent, orally bioavailable human CB1/CB2 dual agonist with antihyperalgesic properties and restricted central nervous system penetration." *Journal of medicinal chemistry* 50, no. 16 (2007): 3851-3856.

a. Acryl fentanyl has an acrylamide electrophilic alkene (C=C double bond), whereas fentanyl has a propanoyl amide.
b. Acryl fentanyl can react with nucleophiles in ways that fentanyl cannot, including amines and thiols (sulfur-based nucleophiles) found in large biomolecules of relevance to drugs of abuse.



methcathinone
controlled substance

pseudoephedrine
(Sudafed)

methamphetamine
controlled substance

37. For context in Analogue determinations, consider that the *chemical functionality / functional group* difference in chemical structure between acryl fentanyl and fentanyl is analogous to the difference between methcathinone and pseudoephedrine (Sudafed).

a. Methcathinone is a Schedule I controlled substance associated with stimulant effects. Pseudoephedrine (Sudafed) is an over-the-counter cold medicine.
b. Pseudoephedrine (Sudafed) has two extra hydrogen atoms and one fewer π-bond as compared to methcathinone. Pseudoephedrine can be converted into methcathinone by the removal of two hydrogen atoms. Pseudoephedrine can be converted into methamphetamine by the removal of one oxygen atom.
c. These chemical structure relationships resulted in pseudoephedrine being listed for restricted access as a controlled substance precursor, but not scheduled itself for controls. The additions or removals of hydrogen and oxygen atoms outlined above are relatively easy to accomplish in a chemistry lab, but they constitute significant changes to the chemical structure.
d. Acryl fentanyl has two fewer hydrogen atoms and one extra π-bond as compared to fentanyl. Acryl fentanyl can be converted into fentanyl by the addition of two hydrogen atoms.

38. In summary, it is my opinion that acryl fentanyl is not substantially similar in chemical structures to fentanyl.

a. The chemical functionalities of these two substances differ in a significant way.
b. The acryl portion of acryl fentanyl is significant.
c. If there is a significant difference between two structures, then the structures are not “substantially similar”.

39. My analyses and opinions would be accepted by the scientific community.